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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/503,387	02/14/2000	Samantha J. Busfield	7853-178	6531

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	19

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/503,387	BUSFIELD ET AL.	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-29,33-47 and 53-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *26-29,33-35,53,65-70,75-77 and 87-90* is/are allowed.

6)☐ Claim(s) *24-25, 36-40, 44-47, 54-64, 71-73, and 80-86* is/are rejected.

7)☒ Claim(s) *41-43,74,78 and 79* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The request filed 9/26/02 for correction of Inventorship Under 37 C.F.R. § 1.48(b) to delete Martine Jandrot-Perrus and William Vainchenker is acknowledged. Said inventors have been deleted.

2. Claims 24-29, 33-47, and 53-90 are pending.

3. The following new grounds of rejection are necessitated by the amendment filed 9/26/02.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 37-39, 55-64, and 80-82 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a composition comprising a substantially purified antibody or fragment thereof that specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 for affinity chromatography, and detection assays; (2) The said composition wherein the antibody is a human antibody; (3) A substantially purified non-human antibody or fragment thereof that specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 for affinity chromatography; (4) A substantially purified non-human monoclonal antibody or fragment thereof that specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 for affinity chromatography; (5) The substantially purified non-human monoclonal antibody or fragment thereof that specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 which is a humanized antibody; (6) A monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with

ATCC as Accession Number 207180; (7) A conjugated monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 wherein the antibody is conjugated to a therapeutic moiety; (8) A conjugated monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 wherein the antibody is coupled to a detectable substance such as an enzyme, a prosthetic group, a fluorescent material, a lumininescent material, and a radioactive material; (9) A substantially purified antibody or a fragment thereof which specially binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or SEQ ID NO: 16; (10) The said antibody wherein the extracellular domain consisting of amino acid residues 21 to 269 of SEQ ID NO: 3 or amino acid residues 22 to 267 of SEQ ID NO: 16, (10) the said antibody wherein the extracellular domain consists of an immunoglobulin-like domain; (11) A substantially purified antibody or a fragment thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or 16 wherein the antibody is a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a humanized antibody, or a human antibody; (12) A conjugated antibody or fragment thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or 16 wherein the antibody is conjugated to a therapeutic moiety, or a detectable substance such as an enzyme, a prosthetic group, a fluorescent material, a luminescent material, a bioluminescent material, and a radioactive material; (13) A kit comprising the antibody mentioned above and instruction for use; (14) A method for making an antibody that specifically recognizes GPVI, the method comprising: a) immunizing a mammal with a polypeptide comprising the amino acid sequence of SEQ IDNO: 3, or the amino acid sequence encoded by the insert of the plasmid deposited with ATCC as Accession Number 207180; and b) collecting a sample from the mammal that contains an antibody that specifically recognizes GPVI; (15) The said method wherein the polypeptide is recombinantly produced; (16) The said method further comprises purifying antibodies from the sample; (17) The said method further comprises collecting a monoclonal antibody-producing cell from the mammal; (18) The said method further comprises collecting monoclonal antibodies which specifically recognize GPVI from the monoclonal antibody-producing cell; (19) The said method wherein the antibody specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or 16; (20) A monoclonal

antibody or fragment thereof which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 or 16, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as PTA-225; (21) A kit comprising a substantially purified non-human antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 wherein the antibody is at least 80%, 90%, 95% or 99% pure and instructions for use in detection assays, **does not** reasonably provide enablement for (1) *any* substantially purified antibody or a fragment thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or 16 wherein the extracellular domain "**comprises**" amino acid residues 21 to 269 of SEQ ID NO: 3 or amino acid residues 22 to 267 of SEQ ID NO: 16 as recited in claim 37; (2) *any* substantially purified antibody or a fragment thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or 16 wherein the extracellular domain "**comprises**" an immunoglobulin-like domain as recited in claim 38; (3) *any* substantially purified antibody or a fragment thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or 16 wherein the extracellular domain "**comprises**" an immunoglobulin-like domain wherein the immunoglobulin-like domain "comprises" amino acid residues such as the ones recited in claim 39; (4) *any* "**pharmaceutical composition**" comprising the composition comprising *any* substantially purified antibody such as the ones recited in claims 55-64, and 80-82 for treating any disease such as the ones disclosed on page 114 of the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only (1) a composition of substantially purified antibodies or fragment thereof which antibodies bind to a polypeptide comprising an amino acid sequence of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 wherein said antibody is conjugated to a therapeutic moiety for targeting therapeutic agent to the platelet receptor, (2) the said antibody is linked to a detectable substance for diagnosis and screening assays and (3) a kit comprising said antibody for diagnosis and screening assays.

The specification does not reasonably provide enablement for *any* substantially purified antibody or any fragment thereof which specifically binds to *any* extracellular domain of the amino acid sequence of SEQ ID NO: 3 wherein the extracellular domain "**comprises**" amino acid residues 21 to 269 of SEQ ID NO: 3, or the said extracellular domain "**comprises**" an immunoglobulin-like domain wherein the immunoglobulin-like domain "comprises amino acid residues 48 to 88 or 134 to 180. The term "comprises" is open-ended. It expands the extracellular domain or the immunoglobulin-like domain of the amino acid sequence of SEQ ID NO: 3 to include additional amino acids at either or both ends in addition to the specific amino acid residues which already recited in SEQ ID NO: 3. There is insufficient guidance as to the binding specificity and the epitope to which the antibody binds. Further, no showing in the specification as filed that any of the claimed antibody such as humanized, chimeric, human antibody, monoclonal antibody ever been made, much less in vivo working example demonstrating any of the "**pharmaceutical composition**" comprising any antibody for treating any disease.

A pharmaceutical composition for treating any disease in the absence of in vivo data is unpredictable for the following reasons: (1) not all antibody can be use for treating *any* disease such as developmental disorders, embryonic disorders, cerebral vascular disease, or pain the antibody may not reach the target area because, i.e. the antibody may not be able to cross the blood brain barrier or may be adsorbed by fluids, cells and tissues where the antibody has no effect; (2) the efficacy of the antibody or Fc fusion polypeptide has not been definitively demonstrated; (3) it is not always possible to extrapolate directly from in vitro experiments to in vivo treatment of all disease; (4) other functional properties, known or unknown, may make the antibody unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Ngo *et al* (of record) teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Kuby et al (of record) teach immunization with a peptide comprising a contiguous amino acid sequence of 8 amino acid residues versus a protein derived from a full-length polypeptide may result in **antibody specificity** that differs from antibody specificity directed against the native full-length polypeptide. Given the lack of guidance as the binding specificity of the claimed antibody, it is unpredictable which undisclosed antibody would bind specifically to the extracellular domain or the immunoglobulin domain "**comprises**" the additional undisclosed amino acid residues, in turn, the antibody would be useful for even diagnosis or screening assays. For these reasons, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention. In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the lack of in vivo working examples, the unpredictability of the art, the in sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 9/26/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 48-52 have been canceled. (2) Claim 65 has been amended and claim 29 recites a monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert…for which the Examiner acknowledges is enabled.

However, claims 55-64, and newly added claims 80-82 recite a pharmaceutical composition. A pharmaceutical composition for treating any disease in the absence of in vivo data is unpredictable for the following reasons: (1) not all antibody can be use for treating *any* disease such as developmental disorders, embryonic disorders, cerebral vascular disease, or pain the antibody may not reach the target area because, i.e. the antibody may not be able to cross the blood brain barrier or may be adsorbed by fluids, cells and tissues where the antibody has no effect; (2) the efficacy of the antibody or Fc fusion polypeptide has not been definitively demonstrated; (3) it is not always possible to extrapolate directly from in vitro experiments to in

vivo treatment of all disease; (4) other functional properties, known or unknown, may make the antibody unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

With regard to claims 37-39, the term "comprises" is open-ended. It expands the extracellular domain or the immunoglobulin-like domain of the amino acid sequence to include additional amino acids at either or both ends in addition to the specific amino acid residues which already recited in SEQ ID NO: 3 or 16. The specification does not reasonably provide enablement for *any* substantially purified antibody or any fragment thereof which specifically binds to *any* extracellular domain of the amino acid sequence of SEQ ID NO: 3 wherein the extracellular domain "**comprises**" amino acid residues 21 to 269 of SEQ ID NO: 3, or the said extracellular domain "**comprises**" an immunoglobulin-like domain wherein the immunoglobulin-like domain "comprises amino acid residues 48 to 88 or 134 to 180. The term "comprises" is open-ended. It expands the extracellular domain or the immunoglobulin-like domain of the amino acid sequence of SEQ ID NO: 3 to include additional amino acids at either or both ends in addition to the specific amino acid residues which already recited in SEQ ID NO: 3. There is insufficient guidance as to the binding specificity and the epitope to which the antibody binds. Further, no showing in the specification as filed that any of the claimed antibody such as humanized, chimeric, human antibody, monoclonal antibody ever been made, much less in vivo working example demonstrating any of the pharmaceutical composition comprising any antibody for treating any disease. Claim 29 is included in this rejection because the pharmaceutical composition of claims 57-58 depends on claim 29.

6. Claims 37-39, 55-64, and 80-82 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* substantially purified antibody or a fragment thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or 16 wherein the extracellular domain "**comprises**" amino acid residues 21 to 269 of SEQ ID NO: 3 or amino acid residues 22 to 267 of SEQ ID NO: 16 as recited in claim 37; (2) *any* substantially purified antibody or a fragment

thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or 16 wherein the extracellular domain "**comprises**" an immunoglobulin-like domain as recited in claim 38; (3) *any* substantially purified antibody or a fragment thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO: 3 or 16 wherein the extracellular domain "**comprises**" an immunoglobulin-like domain wherein the immunoglobulin-like domain "comprises" amino acid residues such as the ones recited in claim 39; (4) *any* "**pharmaceutical composition**" comprising the composition comprising *any* substantially purified antibody such as the ones recited in claims 55-64, and 80-82 for treating any disease such as the ones disclosed on page 114 of the specification.

The specification discloses only (1) a composition of substantially purified antibodies or fragment thereof which antibodies bind to a polypeptide comprising an amino acid sequence of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180 wherein said antibody is conjugated to a therapeutic moiety for targeting therapeutic agent to the platelet receptor; (2) the said antibody is linked to a detectable substance for diagnosis and screening assays and (3) a kit comprising said antibody for diagnosis and screening assays.

Other than the specific antibody that binds to the specific amino acid sequence mentioned above, there is insufficient **written description** about the structure such as the binding specificity of the claimed antibody associated with function of *any* antibody that binds to the extracellular domain "comprises" amino acid residues 21 to 269 of SEQ ID NO: 3, or to *any* extracellular domain "comprises" an immunoglobulin-like domain wherein the immunoglobulin-like domain "comprises" amino acid residues 48 to 88 or 134 to 180 of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180. The term "comprising" is open-ended. It expands the extracellular domain or the immunoglobulin-like domain to include additional amino acids at either end or both ends. Given the inadequate written description about the binding specificity of any antibody and the absence of in vivo working example, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 9/26/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claims 48-52 have been canceled. (2) Claim 65 has been amended and claim 29 recites a monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert...for which the Examiner acknowledges is enabled.

However, there is insufficient **written description** about the structure such as the binding specificity of the claimed antibody associated with function of *any* antibody that binds to the extracellular domain "comprises" amino acid residues 21 to 269 of SEQ ID NO: 3, or to *any* extracellular domain "comprises" an immunoglobulin-like domain wherein the immunoglobulin-like domain "comprises" amino acid residues 48 to 88 or 134 to 180 of SEQ ID NO: 3 or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180. The term "comprising" is open-ended. It expands the extracellular domain or the immunoglobulin-like domain to include additional amino acids at either end or both ends. Given the inadequate written description about the binding specificity of any antibody and the absence of in vivo working example, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 36, 45-46, and 71-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "which is conjugated to a therapeutic moiety" in claims 45 and 72 is improper because dependent claim should be in narrower in scope than the claim to which it depends from.

The "which is linked to a detectable substance" in claims 46 and 73 is improper because dependent claim should be in narrower in scope than the claim to which it depends from.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 24-25, 36-38, 40, 44, 55 and 61-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugiyama *et al* (Blood 69(6): 1712-1720, June 1987; PTO 1449).

Sugiyama *et al* teach a composition of substantially purified antibody such as autoantibody (human antibody) and fragment thereof such as F(ab')2 in PBS, which is a phosphate buffer saline solution and a pharmaceutical acceptable carrier, wherein the reference antibody specifically binds to a collagen receptor on platelet with an apparent molecular weight of 62 KDa from a patient with defective collagen-induced Platelet aggregation and autoimmune thrombocytopenia (See abstract, Materials and Methods, page 1717, column 1, in particular). The reference protein appears to be the same as the claimed polypeptide of SEQ ID NO: 3 that is predicted to be approximately 62 kDa as disclosed on page 3 line 35. Claims 36 and 37 are included in this rejection because the antibody binds to the platelet receptor that is expressed on the cell surface (extracellular domain) and the reference antibody inherently binds to amino acid residues 21 to 269. The term "comprising" is open-ended. It expands the extracellular domain to read on the full-length polypeptide. Claim 38 is included in this rejection because the reference collagen receptor is a member of the immunoglobulin super family having an immunoglobulin-like domain and the immunoglobulin domains are extracellular domain. Claim 40 is included in this rejection because autoantibody is a polyclonal antibody.

While the reference is silent that the protein to which the reference antibody binds has the same amino acid sequence of SEQ ID NO: 3, the specification on page 3, lines 31-35 discloses that the claimed polypeptide TANGO 268 is identical to GPVI; TANGO 268 and GPVI are both recognized by anti-GPVI antibodies and bind to Cvx. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody.

See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 9/26/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) neither Sugiygma nor Gibbins teach an antibody or composition comprising an antibody or a fragment thereof which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 or an extracellular domain thereof, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC as Accession Number 207180, wherein the antibody is substantially purified as recited in claims 24, 26 and 36. The term "substantially purified" means that the antibody contains no more than 30% (by dry weight) of contaminating antibodies (See page 71, lines 13-18 of specification).

However, the reference protein appears to be the same as the claimed polypeptide of SEQ ID NO: 3 that is predicted to be approximately 62 kDa as disclosed on page 3 line 35. Sugiyama *et al* teach a composition of substantially purified antibody such as autoantibody (human antibody) and fragment thereof such as F(ab')2 in PBS, which is a phosphate buffer saline solution and a pharmaceutical acceptable carrier, wherein the reference antibody specifically binds to a collagen receptor on platelet with an apparent molecular weight of 62 KDa from a patient with defective collagen-induced Platelet aggregation and autoimmune thrombocytopenia (See abstract, Materials and Methods, page 1717, column 1, in particular). The term substantially purified as defined in specification still contains 30% contaminating antibodies such as the reference antibody. Further, Sugiyama *et al* teach how to purify antibody such as the IgG and prepare various antibody fragment (See page 1713, Purification of IgG and Preparation of F(ab/)2 fragment, Fab fragment, and Fc fragment, in particular). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., no more than 30% dry weight) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Last but not least, the argument of counsels cannot take the place of objective evidence that the claimed antibody is not the same as the prior art antibody.

11. Claims 24-25, 36-40, 44, 55, and 61-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Gibbins *et al* (FEBS Letters 413: 255-259, 1997; PTO 1449).

Gibbins *et al* teach a substantially purified antibody such as autoantibody anti-GPVI or fragment thereof such as F(ab')2 in Tris-HCl which is a buffer solution and a pharmaceutical acceptable carrier from a patient with defective collagen-induced Platelet aggregation such as autoimmune thrombocytopenia which specifically binds to glycoprotein VI (GPVI) on platelet (See Materials and Methods, first paragraph, page 256, first column, in particular). The reference surface protein is approximately 60 kDa (See page 256, column 1, Fig 1, arrow, in particular) appears to be the same as the claimed polypeptide of SEQ ID NO: 3 as disclosed on page 3 line 35. Claims 36 and 37 are included in this rejection because the antibody binds to the platelet receptor that is expressed on the cell surface (extracellular domain) and the reference antibody inherently binds to amino acid residues 21 to 269. The term "comprising" is open-ended. It expands the extracellular domain to read on the full-length polypeptide. Claim 38 is included in this rejection because the reference collagen receptor is a member of the immunoglobulin super family having an immunoglobulin-like domain and the immunoglobulin domains are extracellular domain. Claim 40 is included in this rejection because autoantibody is a polyclonal antibody.

While the reference is silent that the protein to which the reference antibody binds has the same amino acid sequence of SEQ ID NO: 3, the specification on page 3, lines 31-35 discloses that the claimed polypeptide TANGO 268 is identical to GPVI; TANGO 268 and GPVI are both recognized by anti-GPVI antibodies and bind to Cvx. Therefore the claimed antibody appears to be the same as the prior art antibody. Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 9/26/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) neither Sugiygma nor Gibbins teach an antibody or composition comprising an antibody or a fragment thereof which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 or an extracellular domain thereof, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC as Accession Number 207180, wherein the antibody is substantially purified as recited

in claims 24, 26 and 36. The term "substantially purified" means that the antibody contains no more than 30% (by dry weight) of contaminating antibodies (See page 71, lines 13-18 of specification).

However, the term substantially purified as defined in specification still contains 30% contaminating antibodies such as the reference antibody. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., no more than 30% dry weight) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Finally, the argument of counsels cannot take the place of objective evidence that the claimed antibody is not the same as the prior art antibody.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 24, 36, 45-47, 54, 56, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sugiyama *et al* (Blood 69(6): 1712-1720, June 1987; PTO 1449) or Gibbins *et al* (FEBS Letters 413: 255-259, 1997; PTO 1449) each in view of Harlow *et al* (in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 321-358) or US Patent No 5,877,289, (March 1999PTO 892).

The teachings of Sugiyama *et al* and Gibbins *et al* have been discussed supra.

The claimed invention as recited in claim 45 differs from the references only by the recitation of the antibody is conjugated to a therapeutic moiety.

The claimed invention as recited in claim 46 differs from the references only by the recitation of the antibody is linked to a detectable substance.

The claimed invention as recited in claim 47 differs from the references only by the recitation of the detectable substance is an enzyme, a prosthetic group, a fluorescent material, a luminescent material, a bioluminescent material and a radioactive material.

The claimed invention as recited in claim 54 differs from the references only by the recitation of a kit comprising an antibody or fragment thereof and instruction for use.

The claimed invention as recited in claim 56 differs from the references only the pharmaceutical composition comprising an antibody, a therapeutic moiety and a pharmaceutical acceptable carrier.

The claimed invention as recited in claim 63 differs from the references only that a pharmaceutical composition comprising an antibody or fragment conjugated to a therapeutic moiety.

The claimed invention as recited in claim 64 differs from the references only by the recitation of a therapeutic moiety.

Harlow *et al* teach methods of labeling any antibody with a detectable substance such as ^{125}Iodine which is a radioactive material widely used for autoradiographic detection and a therapeutic moiety for nuclear medicine (See page 591 and 324, in particular), an enzyme label such as alkaline phosphatase (page 597, in particular), horseradish peroxidase, a fluorescein label such as isothiocynate (FITC) (See page 353, in particular). The advantages of Iodine labeling is that it is easy to quantitative, easy to label directly whereas the advantages of antibody labeled with enzyme include long shelf life, high sensitivity, direct visualization possibility (See page 322, in particular). The fluorescein labeled antibodies offer the advantages of longer shelf life, good resolution, and quantitative analysis.

The '289 patent teaches conjugated antibody from unconjugated antibody such as VEGF antibody conjugated to one or more therapeutic agents such as immunotoxin, chemotherapeutic drugs or diagnostic agents, various tissues factors, biological agents, or enzymes via cleavable peptide linkers as a fusion protein (See column 9-13; column 48-53; column 54-57 paragraph recombinant fusion proteins; column 44, paragraph 2; column 74, paragraph recombinant human truncated tissue factor; column 83-92) and a pharmaceutical composition comprising additional

therapeutic agents such as cyclosporin (See column 12, lines 31-52, columns 72-73, Therapeutic Kits). The '289 patent teaches conjugated antibodies or specific targeting ligands could be used to direct the therapeutic agents to the site of interest (See column 45, lines 40-55, in particular). The '289 patent further teaches the method of detection is conveniently provided in the form of a kit that is a packaged collection of reagents or combination of other assay components as necessary and appropriate for the needs of the user (See columns 72-73, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to link or conjugate the antibody to a detectable substance as taught by Harlow *et al* or therapeutic moiety as taught by '289 patent with the antibody as taught by Sugiyama *et al* and Gibbins *et al* and place the labeled antibody in a kit as taught by '289 patent for convenience and commercial expedience. From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Harlow *et al* teach the advantages of Iodine labeling is that it is easy to quantitative, easily to labeling directly whereas the advantages of antibody labeled with enzyme include long shelf life, high sensitivity, direct visualization possibility; the fluorescein labeled antibodies offer the advantages of longer shelf life, good resolution, and quantitative analysis (See page 322, in particular). The '289 patent teaches conjugated antibodies or specific targeting ligands could be used to direct the therapeutic agents to the site of interest (See column 45, lines 40-55, in particular). A kit will allow for ease of use for the practitioner since all the necessary reagents, standard and instructions for use are included in a kit as taught by '289 (See column 9, lines 46-51, in particular).

Applicants' arguments filed 9/26/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) neither Sugiygma nor Gibbins teach an antibody or composition comprising an antibody or a fragment thereof which specifically binds to a polypeptide comprising the amino acid sequence of SEQ ID NO: 3 or an extracellular domain thereof, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC as Accession Number 207180, wherein the antibody is substantially purified as recited in claims 24, 26 and 36. The term "substantially purified" means that the antibody contains no more than 30% (by dry weight) of contaminating antibodies (See page 71, lines 13-18 of

specification). The combination of the references does not even rise to the level of suggesting or providing motivation the claimed invention.

However, the term substantially purified as defined in specification still contains 30% contaminating antibodies such as the reference antibody. Further, Sugiyama *et al* teach how to purify antibody such as the IgG and prepare various antibody fragment (See page 1713, Purification of IgG and Preparation of F(ab/)2 fragment, Fab fragment, and Fc fragment, in particular). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., no more than 30% dry weight) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Last but not least, the argument of counsels cannot take the place of objective evidence that the claimed antibody is not the same as the prior art antibody.

15. Claims 24, and 83-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sugiyama *et al* (Blood 69(6): 1712-1720, June 1987; PTO 1449) or Gibbins *et al* (of record, FEBS Letters 413: 255-259, 1997; PTO 1449).

The teachings of Sugiyama *et al* and Gibbins *et al* have been discussed supra.

The claimed invention as recited in claim 83 differs from the references only by the recitation that the antibody is at least 80% of total antibodies in the composition.

The claimed invention as recited in claim 84 differs from the references only by the recitation that the antibody is at least 90% of total antibodies in the composition.

The claimed invention as recited in claim 85 differs from the references only by the recitation that the antibody is at least 95% of total antibodies in the composition.

The claimed invention as recited in claim 86 differs from the references only by the recitation that the antibody is at least 99 % of total antibodies in the composition.

Sugiyama *et al* teach a method of purifying antibody (See page 1713, Purification of IgG, in particular) for use in a composition comprising various platelet inhibitors such as the ones shown in Table 2. (See page 1716, Fig 3, Table 2, in particular).

Gibbins *et al* teach a method of purifying antibody (See page 1713, Purification of IgG, in particular) for use in a composition comprising the reference anti-GPVI IgG antibody and

platelet lysate (See page 256, column 2, Immunoprecipitation and immunoblotting studies, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to purify any antibody in a composition as taught by Sugiyama *et al* or Gibbins *et al* to homogeneity such that the antibody composition comprising at least 80%, 90%, 95% or 99% pure. The recitation of a composition comprising 80%, 90%, 95% or 99% of the total antibodies in a composition is well within the purview of one ordinary skill in the art at the time the invention was made to purify or to include additional reagents in any composition as taught by the Sugiyama *et al* and Gibbins *et al*.

16. Claims 26-29, 33-35, 53, 65-70, 75-77 and 87-90 are allowed.

17. Claims 41-43, 74 and 78-79 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are

unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

20. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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Technology Center 1600
December 16, 2002

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